DOI: 10.7860/IJARS/2018/37297:2417

Case Report

Ophthalmology Section

Oculodentodigital Dysplasia (ODDD) Presenting as Bilateral Advanced Glaucoma-A Case Report

ABHISHEK ANAND, NISHA AGGARWAL, MAMTA SINGH, ATUL KUMAR ANAND, ANKITA RATHI

ABSTRACT

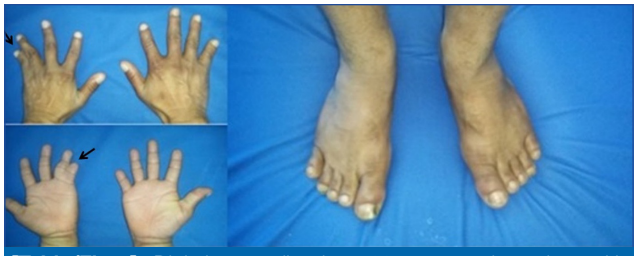
Oculodentodigital dysplasia (ODDD) is a rare multisystem genetic disorder with reported incidence of 1 in 10 million and is known to be associated with microphthalmia and Angle closure glaucoma. Although, extremely rare patients can present in eye out patient department with primary ophthalmic manifestations. We present a case of 38 years old male who presented with complaint of bilateral progressive diminution of vision and advanced glaucoma. Patient also had digital anomalies like syndactyly, and hypoplastic middle phalanx of 5th finger. On dental consultation he was found to have multiple caries, missing teeth and enamel hypoplasia. Patient underwent Bilateral Trabeculectomy with Mitomycin C (MMC) for management of uncontrolled high Intraocular Pressure (IOP).

Keywords: Angle closure glaucoma, Enamel hypoplasia, Syndactyly

CASE REPORT

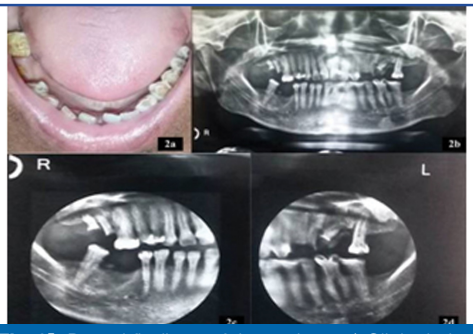
A 38-year-old male presented with painful diminution of vision of both eyes for 3-4 months. After taking informed consent, examination was done. General examination revealed a short statured man with slender nose, hypoplasia of alae of nose, anteverted nares, and prominent columella nasi. He demonstrated dental manifestations like partial anodontia, enamel hypoplasia, microdontia and caries in multiple teeth. On further inquisition, it was noted that he had syndactyly of 4th and 5th fingers, and hypoplasia of middle phalanx of 5th finger [Table/Fig-1,2].

On Ocular Examination, Best Corrected Visual Acuity (BCVA) was 6/18 and 3/60 in Right and Left Eye (RE, LE) respectively. Both were microphthalmic eyes with microcornea having horizontal diameter 10 mm and vertical diameter 9.5 mm. Inter canthal distance was normal. Extra ocular movement was normal. Anterior chamber was Von-Herrick's Grade 1. RE pupillary reaction was normal while LE had Relative Afferent Pupillary Defect (RAPD). IOP was 47 mmHg in RE and 51 mmHg in LE with applanation tonometer. Gonioscopy revealed Angle Closure (Grade 0 by Schaffer's grading) in Both Eyes (BE). Vitreous and macula were normal, C:D ratio was 0.9:1 with thin neuro-retinal rim in BE. The peripheral fundus was within normal limit. Axial length was recorded as 19.81 mm (RE) and 19.73 mm (LE) by Ultrasound (USG) A scan. The



[Table/Fig-1]: Digital anomalies in a 38 years male patient with Oculodentodigital dysplasia-a,b) Syndactyly of 4th and 5th digit of the left hand (black arrow) and middle phalanx of 5th digit of both the hands was hypoplastic; c) Clinical photograph of foot reveals same length of 2nd and 3rd toes.

[Table/Fig-2]: Facial features showing slender Parrot-beaked nose, hypoplasia of alae of the nose, anteverted nares, prominent columella, hypoplastic alae nasi, small anteverted nares and prominent mandible and sparse, laterally absent eye brows.



[Table/Fig-3]: Dental findings of the patient- a) Clinical photograph ; b) Orthopantomogram; c,d) Cropped orthomopentogram right and left jaw respectively reveal missing 46, root stumps with respect to 17,24,25,26 and restoration on 14,15,27,36,37 and 45 suggestive of early caries involvement. There is generalised thinning of enamel suggestive of enamel hypoplasia.

Retinal-Choroidal-Scleral Complex (RCS) thickness was 1.50 mm (RE) and 1.60 mm (LE) respectively.

Dental consultation was seeked and oral findings were confirmed on Orthopantomogram (OPG) which revealed missing 46, root stumps with respect to 17,24,25,26 and restoration on 14,15,27,36,37 and 45 suggestive of early caries involvement. There was generalised thinning of enamel suggestive of enamel hypoplasia [Table/Fig-3].

After analysing clinical features, radiological characteristics and interdepartmental consultations a provisional clinical diagnosis of ODDD was reached.

Very limited literatures and that too few case reports exist regarding the management of Bilateral Advanced ACG in patients with ODDD. Young age, Micropthalmos with medically uncontrolled IOP were added risk factors. However, RCS thickness was within normal limits. Patient was planned for Bilateral Anti-Metabolite (MMC) modulated trabeculectomy considering young age of the patient. Considering the high risk of intraoperative Choroidal Detachment (CD) or Choroidal Haemorrhage (CH) pre-operatively patient was given intravenous mannitol (20%, 200cc) and was started on oral (Tablet Diamox) and topical antiglaucoma medications pre-operatively. Peribulbar block with plain lignocaine and bupivacaine (5 mL, 1:1 mixture) with hyaluronidase was given.

Anterior chamber maintainer was used considering the risk for sudden decompression and to avoid secondary CD or CH. Fornix based conjunctival flap along with Tenon's capsule was dissected and light cautery was used to achieve haemostasis. Sub-conjunctival Mitomycin C (0.2 mg/ml MMC applied for 2 minutes) was used. A thorough wash with 20% ringer lactate was given. Scleral flap 4×4 mm was than dissected till the entry into clear cornea. After resection of anterior trabecular block (2.5×1 mm) a peripheral iridectomy was performed. Scleral flap was sutured with 10-0 nylon sutures at two corners. Two anchoring sutures with 10-0 nylon suture was taken at the corner of limbal flaps to achieve tight apposition and no visible leak. Postoperative topical corticosteroids (prednisolone acetate) and antibiotic drops were given four to six times a day for a maximum period upto six weeks. Intraoperative period was uneventful in both the eyes. Post operatively at one month visual acuity remained static and IOP was 11 and 12 mmHg in RE and LE respectively without anti-glaucoma medications.

DISCUSSION

ODDD is an extremely rare multisystem genetic disorder of gap junction protein mutation with only 300 cases reported worldwide. The incidence of this rare disorder is around 1 in 10 million [1].

The condition is also known as oculo-dento-osseous syndrome or Meyer-Schwickerath syndrome [2]. Lohmann first described this disorder in 1920 [3]. This is an autosomal dominant disorder with high penetrance and variable expressions [4], but it may be sporadic or autosomal recessive in nature as well [5,6]. Both the genders are equally affected [4]. Some features of ODDD are evident at birth, while others become apparent mainly in the second decade of life [3,7]. It has been observed more commonly in Indo-Europeans than in Asian or African population. In familial cases, male:female ratio was found nearly 1:1 while and it was about 6:15 in sporadic cases [4]. The cause of female predominance was attributed to male embryonic lethality or greater societal recognition of female facial features [6].

ODDD occurs due to mutation in *GJA1* gene located on human chromosome *6q22-q23*, encoding *Connexin43 (Cx43)* [8,9]. *Cx43* is found in intercellular channels of gap junction in many tissues throughout the body. This mutation causes alteration in cell conduction property at the gap junctions. Therefore, the gap junctions are permanently closed leading to disrupted morphological patterning during development and altered functioning of cells in mature state [4].

It is marked by pleiotropic arrays of developmental anomalies mainly affecting- eyes (oculo), teeth (dento), fingers and toes (digital). Less common features include camptodactyly, clinodactyly, syndactyly of the toes, microcephaly, cleft palate, conductive hearing loss, neurological and cardiac problems [4].

In 92% of cases, characteristic facial appearance is evident [9]. These include thin/narrow nose with hypoplastic alae nasi, thin nostrils, small anteverted nares, and/or prominent columnella along with microcephaly [4,10]. Hair and nails are brittle with abnormalities of hypotrichosis and slow growth reported in 26% of the affected families [4,9].

Ocular features are found in 68% of cases [9]. Commonly evident ocular manifestations are short palpebral fissure, epicanthal fold, hyper/hypotelorism, microphthalmia,

microcornea and fine porous spongy iris abnormalities. Sometimes gaze palsies and squinting may occur. Blindness develops due to glaucoma, cataract or optic atrophy in some of the patients. The risk of glaucoma is approximately eight-fold more in ODDD individuals than the general population (16% vs. 1.86%) [11]. Our patient had Chronic Angle Closure Glaucoma (CACG) in both the eyes. Currently, there are very few cases in literature describing CACG in ODDD. One case reported recently was of severe angle closure glaucoma secondary to ciliary body cyst [12]. However, no such cause could be identified in our patient. Conductive hearing loss and dysplastic ears may be present as rare as in 26% of affected families [9,10].

Oral abnormalities in primary and permanent dentition with microdontia, partial anodontia, enamel hypoplasia, numerous caries and early tooth loss were more common and were evident in 70% of the cases [9].

Digital anomalies were evident in 80% of the cases [10] which included syndactyly involving 3rd, 4th & 5th fingers and 2nd to 4th toes, camptodactyly and clinodactyly owing to hypoplasia or aplasia of the middle phalanges [13]. However, our patient did not manifest with any fusion of the toes.

Neurological symptoms are seen in only 30% of the affected families [9]. If present it includes dysarthria, spastic paraparesis, ataxia, neurogenic bladder disturbances, anterior tibial muscle weakness and [14]. Differential diagnosis includes Orofaciodigital syndrome Type II, Hallermann-Streiff syndrome, Axenfeld Rieger Syndrome, Ectrodactyly Ectodermal Dysplasia Clefting (EEC) syndrome [3].

Our case was probably sporadic as no history of any similar features noted in any of the parents. Finally, ODDD diagnosis was done by ruling out other similar syndromes by evaluating clinical findings and investigation reports through concerned multidisciplinary approach. Patient was advised for genetic testing and detailed systemic evaluation, but he refused.

Management of such cases requires joint efforts from physician from various departments. Cardiac and neurological intervention depends on discretion of the treating physician. Early recognition and treatment of ocular symptoms can salvage vision. Preventive and therapeutic dental treatment depends on the age of the patient [6]. A conservative approach should be taken to maintain the integrity and aesthetics of the patient's permanent dentition [15]. Digital anomalies need to be corrected surgically for better function and cosmesis [16].

CONCLUSION

ODDD is a relatively rare disorder which can go unrecognised many a times. We have reported a case of ODDD who presented with advanced angle closure glaucoma. This case is unique because of rarity of ODDD itself and even rarer is its presentation with advanced glaucoma.

ABBREVIATIONS

BCVA: Best Corrected Visual Acuity

RE, LE, BE: Right Eye, Left Eye, Both Eyes

IOP: Intraocular Pressure

C/D: Cup/Disc

USG: Ultrasound

RCS complex: Retinal-Choroidal-Scleral Complex

OPG: Orthopantomogram

MMC: Anti-Metabolite Modulated Trabeculectomy

CD: Choroidal Detatchment

CH: Choroidal Hemorrhage

Cx43: Connexin43

CACG: Chronic Angle Closure Glaucoma

EEC: Ectrodactyly Ectodermal Dysplasia Clefting

REFERENCES

[1] Parashari UC, Khanduri S, Bhadury S, Qayyum FA. Radiographic diagnosis of a rare case of oculodentodigital dysplasia. SA J Radiol. 2011;15(4):134-36.

[2] Alao MJ, Bonneau D, Holder-Espinasse M, Goizet C, Manouvrier-Hanu S, Mezel A, et al. Oculo-dento-digital dysplasia: Lack of genotype-phenotype correlation for GJA1 mutations and usefulness of neuro-imaging. Eur J Med Genet. 2010;53(1):19-22.

[3] Mubeen K, Vijyalakshmi KR, Ohri N, Gohli NR. Oculo-dento-digital dysplasia: An interesting case. Indian J Ophthalmol. 2016;64(3): 227-30.

[4] Paznekas WA, Boyadjiev SA, Shapiro RE, Daniels O, Wollnik B, Keegan CE, et al. Connexin 43 (GJA1) mutations cause the pleiotropic phenotype of oculodentodigital dysplasia. Am J Hum Genet. 2003;72(2):408-18.

[5] Frasson M, Calixto N, Cronemberger S, Aguiar RALP, Leão LL, Aguiar MJB. Oculodentodigital dysplasia: study of ophthalmological and clinical manifestations in three boys with probably autosomal recessive inheritance. Ophthalmic Genetics. 2004;25(3):227-36.

[6] Kayalvizhi G, Subramaniyan B, Suganya G. Clinical manifestations of oculodentodigital dysplasia. J Indian Soc Pedod Prev Dent. 2014;32(4):350-52.

[7] Oculodentodigital dysplasia. Genetic Home Reference (GHR) 2009. https://ghr.nlm.nih.gov/condition/oculodentodigital-dysplasia. [Accessed on 18/1/2018].

[8] Dobrowolski R, Sommershof A, Willecke K. Some oculodentodigital dysplasia-associted Cx43 mutations cause increased hemichannel activity in addition to deficient gap junction channels. J Membr Biol. 2007;219(1-3):9-17.

[9] Paznekas WA, Karczeski B, Vermeer S, Lowry RB, Delatycki M, Laurence F, et al. *GJA1* mutations, variants, and *connexin 43* dysfunction as it relates to the oculodentodigital dysplasia phenotype. Hum Mutat. 2009;30(5):724-33.

[10] Kjaer KW, Hansen L, Eiberg H, Leicht P, Opitz JM, Tommerup N. Novel *connexin 43 (GJA1)* mutation causes oculo-dento-digital dysplasia with curly hair. Am J Med Genet A. 2004 ;127A(2):152-57.

[11] Friedman DS, Wolfs RC, O'Colmain BJ, Klein BE, Taylor HR, West S, et al. Prevalence of open-angle glaucoma among adults in the United States. Arch Ophthalmol. 2004;122(4):532-38.
[12] Mosaed S, Jacobsen BH, Lin KY. Case report: imaging and treatment of ophthalmic manifestations in oculodentodigital dysplasia. BMC Ophthalmol. 2016;16:5.
[13] Vitiello C, D'Adamo P, Gentile F, Vingolo EM, Gasparini P, Banfi S. A novel *GJA1* mutation causes oculodentodigital dysplasia without syndactyly. Am J Med Genet A. 2005;133A(1):58-60.
[14] Loddenkemper T, Grote K, Evers S, Oelerich M, Stögbauer F. Neurological manifestations of the oculodentodigital dysplasia syndrome. J Neurol. 2002;249(5):584-95.
[15] Aminabadi NA, Pourkazemi M, Oskouei SG, Jamali Z. Dental management of oculodentodigital dysplasia:a case report. J Oral Sci. 2010;52(2):337-42.
[16] Thomsen M, Schneider U, Weber M, Niethard FU. Different appearance of Oculodentodigital Dysplasia Syndrome. J Pediatr Orthop B. 1998;7(1):23-26.

AUTHOR(S):
1. Dr. Abhishek Anand
2. Dr. Nisha Aggarwal
3. Dr. Mamta Singh
4. Dr. Atul Kumar Anand
5. Dr. Ankita Rathi

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Ophthalmology, AIIMS, Patna, Bihar, India.
2. Fellow, Department of Ophthalmology, Biratnagar, Eye Hospital, Biratnagar, Nepal.
3. Senior Resident, Department of Ophthalmology, Patna, Medical College and HospitaL, Patna, Bihar, India.
4. Senior Resident, Department of Ophthalmology, AIIMS, Patna, Bihar, India.
5. Postgraduate, Department of Pedodontics and Maxillofacial Prosthetics, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Abhishek Anand,
Flat No. 204, Ganga 4, Jalalpur City, Gola Road,
Patna-801503, Bihar, India.
E-mail: eyehospitalpatna@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Publishing: **Jul 01, 2018**